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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/617,334	HAYDEN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2008 and 26 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,29-40,46-61 and 63-68* is/are pending in the application.

4a) Of the above claim(s) *1-23,29-40,46-48 and 50-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,49,57-61 and 63-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-27, 29-40, 46-61, and 63-68 are pending in the application.

[2] Applicant's amendment to the claims, filed on 12/1/08, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's remarks filed on 12/1/08 in response to the Office action mailed on 5/28/08 have been fully considered and are deemed to be persuasive to overcome at least one of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[5] Applicant's election of species (A), a compound that binds to an ABC1 polypeptide, in the reply filed on 2/26/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

[6] Claims 1-23, 29-40, 46-48, and 50-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/6/2006.

[7] Claims 24-27, 49, 57-61, and 63-68 are being examined to the extent the claims read on the elected subject matter of Group V of the restriction requirement as set forth in the Office action mailed on 12/29/05.

Claim Rejections - 35 USC § 112, First Paragraph

[8] The new matter rejection of claims 24-27, 49, 57-61, and 63-68 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the instant amendment to claim 24 to replace "an agent" with "a compound".

[9] Claims 24-27, 49, 57-61, and 63-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 24 is drawn to a method to increase plasma HDL-C in a human by administering a genus of compounds that increase ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide. Thus, a compound that binds to an ABC1 polypeptide and increases ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human is required to practice the invention. The specification does not describe an actual reduction to practice of a method of increasing plasma HDL-C in a human by

administering a compound that increases ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide.

The specification also does not describe the complete structure of a compound that increases ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide. Further, the specification does not describe the partial structures, or physical properties, or chemical properties of a compound that increases ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide. While the specification describes the amino acid sequence of the human ABC1 polypeptide of SEQ ID NO:1, the specification does not describe any correlation between the sequence of SEQ ID NO:1 and the structure of any compounds that increase ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide. The specification describes a method of screening compounds for those that have agonist activity toward an ABC1 polypeptide (pp. 50-51) and further discloses a method of screening compounds for those that bind to ABC1 polypeptide (pp. 61-62); however, there is no information regarding what structural features would likely be associated with the genus of recited compounds. Thus, the specification does not disclose a correlation between the activity of binding to ABC1 and increasing ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human and the structure of a putative compound. The level of skill and knowledge in the art is that there are no known

compounds that bind to ABC1 and increase ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human. See, *e.g.,* the reference of Nofer et al. (*Cell Mol Life Sci* 62:2150-2160, 2005; cited as reference U in the Form PTO-892 mailed on 5/31/06), which discloses that a therapeutic for targeting ABCA1 in the treatment of coronary heart disease "has not yet been fulfilled". Also, there is no known correlation between any structural component and the ability to bind to ABC1 and increase ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human. Thus, the disclosure does not allow one of skill in the art to visualize or recognize the structure of any compound required to practice the claimed method. Accordingly, one of ordinary skill in the art would conclude that the applicant would not have been in possession of the claimed method of increasing plasma HDL-C in a human by administering a genus of compounds that increase ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide because a compound possessing the desired activity required to practice the method is not adequately described and was not known in the art.

RESPONSE TO ARGUMENT: At p. 10 of the instant remarks, applicant argues the rejection is obviated by amendment "to more succinctly recite the claimed invention and clearly defined the agents whose use is intended". According to applicant, a skilled artisan would recognize the genus of compounds does not encompass antisense

molecules and antibodies because the specification discloses evidence that these agents decreased ABC1 activity.

Applicant's argument is not found persuasive. The claim amendment is acknowledged. However, at least for the reasons of record and the reasons set forth above, the examiner maintains the position that the specification fails to show that applicant was in possession of the claimed invention, particularly with respect to the genus of recited compounds. That the specification provides only a research plan for identifying the recited genus of compounds is evidenced by the instant remarks in addressing the scope of enablement rejection, namely that the disclosed assays facilitate the identification of the compounds to practice the claimed invention (instant remarks, p. 13, top) and that analogs of cholesterol and HDL are likely starting points for screening compounds that are encompassed by the claimed method (instant remarks, p. 11, middle). However, MPEP 2163.II.A.2.(a) makes clear that "[a]n adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and *not merely a wish or plan for obtaining the chemical invention claimed*. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004)" (emphasis added).

[10] Claims 24-27, 49, 57-61, and 63-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

(A) The breadth of the claims: According to MPEP 2164.04, "[b]efore any analysis of enablement can occur, it is necessary for the examiner to construe the claims…and explicitly set forth the scope of the claim when writing an Office action." Also, MPEP 2164.08 states, "[a]ll questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject matter is encompassed by the

claims…claims are to be given their broadest reasonable interpretation that is consistent with the specification."

As noted above, claim 24 (claims 25-27, 49, 57-61, and 67-68 dependent therefrom) is drawn to a method to increase plasma HDL-C in a human by administering a compound that increases ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human, where the compound binds to an ABC1 polypeptide. Thus, a compound that binds to an ABC1 polypeptide and increases ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human is required to practice the invention. Claims 63 and 64 require the ABC1 lipid transport activity to be at least 25% and 50%, respectively. Claims 65 and 66 require the plasma HDL-C to be increased by at least 25% and 50%, respectively. The structure of the compound is unlimited.

RESPONSE TO ARGUMENT: At p. 11 of the instant remarks, in addressing the breadth of the claims, applicant argues claim 24 has been amended to limit the method to using a compound that binds to ABC1 polypeptide.

The examiner acknowledges applicant's amendment to the claim. It is noted that the recited compound, while being limited to a compound that binds to an ABC1 polypeptide, is further required to increase ABC1 lipid transport activity in fibroblasts and macrophages by at least 10% in a human.

(C) The state of the prior art; (D) The level of one of ordinary skill; and (E) The level of predictability in the art: According to MPEP 2164.03, "…what is known in the art

provides evidence as to the question of predictability." At the time of the invention, neither the specification nor the prior art discloses a method for providing any treatment in a human having or at risk of developing a cardiovascular disease by increasing by at least 10%, 25%, or 50% the level of ABC1 lipid transport activity in the human. Even *after* the time of the invention the art recognizes that a therapeutic targeting ABCA1 for the treatment of coronary heart disease "has not yet been fulfilled" (Nofer et al. *Cell Mol Life Sci* 62:2150-2160, 2005; p. 2156, right column, bottom), providing evidence of a high level of unpredictability for practicing the claimed method. While Nofer et al. acknowledges that "such treatments may be on the horizon," the reference also acknowledges that at least one potential therapy, namely LXR agonists, may cause gene changes that are detrimental (p. 2157, left column, top). In this case, the specification and/or prior art fail to set forth even a single method for achieving an increase in ABC1 lipid transport activity of at least 10% to provide a treatment to a human.

RESPONSE TO ARGUMENT: At p. 11 of the instant remarks, in addressing the state of the art and the level of skill and predictability, applicant argues the advantage of the disclosure is in knowing the specific activity of ABC1 that is to be modulated. Applicant argues that since the specification discloses the role of ABC1 in cholesterol transport and HDL binding of cholesterol, "then clearly analogs of cholesterol and HDL are likely starting points" and that "numerous compounds are readily prepared and tested". According to applicant, the claims are not drawn to a method of using a specific compound, but rather to "a way of treating".

Applicant's argument is not found persuasive. There appears to be no dispute that the prior art fails to disclose even a single compound as encompassed by the claimed method. Instead, it appears that applicant takes the position that a skilled artisan can make and test such compounds for those that have the desired activity. However, at the time of the invention, there is no evidence of record to suggest that such a compound existed or could have been made and based on the noted teachings of Nofer, even after the time of the invention, making such a compound had yet to be achieved.

(F) The amount of direction provided by the inventor and (G) The existence of working examples: The specification fails to disclose even a single working example of the claimed method that achieves an increase of at least 10% of ABC1 lipid transport activity in an affected human as encompassed by the claims. While it is acknowledged that MPEP 2164.02 states, "[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed," this same section of MPEP makes clear that "[l]ack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art." While the specification discloses general methods for, *e.g.,* isolating compounds that may achieve the desired increase in ABCA1 lipid transport activity, such guidance amounts to a trial and error research plan without providing any specific guidance regarding those compounds that are likely to be successful for practicing the claimed method. The specification fails to provide guidance regarding, *e.g.,* production of the

compound and, if the compound is a polypeptide, the associated potential for antigenic effects in a human, whether or not the polypeptide has ABC1 binding activity without further processing or post-translational modification, stability/turnover of the compound, formulation of the compound for administration, routes of administration, and dosage level required to achieve increased ABC1 lipid transport activity by at least 10%, 25%, or 50% in fibroblasts or macrophages of a human, which are all relevant considerations for a therapeutic. In this case, in view of the high level of unpredictability and lack of guidance provided in the specification, a skilled artisan would have no expectation that such a method can be achieved.

RESPONSE TO ARGUMENT: Beginning at p. 11 of the instant remarks, in addressing the direction provided by the inventor and the working examples, applicant argues the disclosure's key teaching is the determination of physiological role of ABC1 in lipid transport. Applicant argues the specification discloses screening assays to identify compounds used in the claimed method.

Applicant's argument is not found persuasive. There appears to be no dispute that the specification fails to disclose even a single compound as encompassed by the claimed method. Instead, it appears that applicant takes the position that a skilled artisan can make and test such compounds for those that have the desired activity. However, at the time of the invention, there is no evidence of record to suggest that such a compound existed or could have been made, particularly as the specification fails to disclose even a single working example of such a compound, much less *any* compound as broadly encompassed by the claims.

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of treatment of a cardiovascular disease were known in the art at the time of the invention, it was not routine to experiment to identify a method for increasing by at least 10%, 25%, or 50% the ABCA1 lipid transport activity in a human using an as yet unidentified compound that binds to ABC1 and increases ABC1 lipid transport activity by at least 10%.

RESPONSE TO ARGUMENT: Beginning at p. 12 of the instant remarks, in addressing the amount of experimentation required, applicant argues Table 1 of the Bamberger patent (US Patent 6,555,323) identifies compounds that increase ABC1 activity and were identified using essentially the same methods as disclosed in the instant specification, thereby indicating that the disclosure "clearly facilitate[s] ready identification of positive modulators of ABC1 activity".

Applicant's argument is not found persuasive. It should be noted that applicant does not appear to rely on the '323 patent as showing that compounds encompassed by the claims were known in the art at the time of the invention. This is because the '323 patent has an effective filing date that is after the effective filing date of the instant application and thus the disclosure of the '323 patent was not available to a skilled artisan at the time of the instant invention. Instead, it appears applicant relies on the '323 patent to support a position that the experimentation involved in making the recited compounds is not undue, using screening methods that require only routine experimentation. However, there is no evidence of record that would suggest that at the

time of the invention, a compound or compounds that bind to ABC1 and increase ABC1 lipid transport activity by at least 10%, 25%, or 50% in fibroblasts or macrophages in a human could have been achieved by using the disclosed screening assays. Even the post-filing evidence of the '323 patent fails to demonstrate the existence of a compound that binds to ABC1 and increases ABC1 lipid transport activity by at least 10%, 25%, or 50% in fibroblasts or macrophages in a human.

Conclusion

[11] Status of the claims:

- Claims 1-27, 29-40, 46-61, and 63-68 are pending.
- Claims 1-23, 29-40, 46-48, and 50-56 are withdrawn from consideration.
- Claims 24-27, 49, 57-61, and 63-68 are rejected.
- No claim is in condition for allowance.

This is a continued examination application. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656